

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (previously presented). A pharmaceutical composition comprising an apolipoprotein protein construct having the general formula

- apo-A-X,
- where apo-A is an apolipoprotein component selected from the group consisting of apolipoprotein A_I, apolipoprotein A_{II}, and apolipoprotein A-IV,
- and X is a tetranectin trimerising module.

2 (previously presented). The composition of claim 1, further comprising a spacer peptide between the apo-A component and the tetranectin trimerising module, wherein the spacer peptide comprises at least two amino acids.

3 (previously presented). The composition according to claim 2, wherein the spacer peptide is essentially non-immunogenic, and/or is not prone to proteolytic cleavage and/or does not comprise any cystein residues.

4 (previously presented). The composition according to claim 2, wherein the three-dimensional structure of the spacer is linear.

5 (previously presented). The composition according to claim 2, wherein the spacer peptide comprises an amino acid sequence selected from the group consisting of GTKVHMK (SEQ ID NO:69) PGTSGQQPSVGQQ (SEQ ID NO:70), GTSGQ (residues 2-6 of SEQ ID

Appln. No. 09/987,107
Amd. dated August 11, 2004
Supplementing Reply to Office Action of February 11, 2004

NO:70), PKPSTPPGSS (SEQ ID NO:71), SGGTSGSTSGTGST (SEQ ID NO:72), AGSSTGSSTGPGSTT (SEQ ID NO:73) and GGSGGAP (SEQ ID NO:74).

6 (previously presented). The composition of claim 1, wherein the tetranectin trimerising module is linked by a covalent link to the N-terminal or the C-terminal amino acid of apo-A.

7-21 (cancelled).

22 (previously presented). The composition of claim 1, wherein the tetranectin trimerising module is part of a stable trimeric complex with two other tetranectin trimerising modules.

23 (previously presented). The composition of claim 22, wherein the stable trimeric complex includes a coiled coil structure.

24 (original). The composition of claim 23, wherein the coiled coil structure is a triple alpha helical coiled coil.

25 (previously presented). The composition of claim 22, wherein the stable trimeric complex comprises two tetranectin trimerising modules linked by a spacer moiety, which allows both of the two tetranectin trimerising modules to take part in the complex formation with a third tetranectin trimerising module not being part of the apolipoprotein protein construct.

26 (previously presented). The composition of claim 1, wherein the tetranectin trimerising module is selected from

Appln. No. 09/987,107
Amd. dated August 11, 2004
Supplementing Reply to Office Action of February 11, 2004

the group consisting of human tetranectin, murine tetranectin or C-type lectin of human, bovine or shark cartilage.

27 (previously presented). The composition of claim 1, wherein the tetranectin trimerising module comprises a sequence having at least 68% identity with the sequence of SEQ ID NO 12 and is capable of forming a stable trimeric complex with other tetranectin trimerising modules.

28 (previously presented). The composition of claim 27, wherein the cysteine residue 50 in SEQ ID NO 12 is substituted by a serine residue, a threonine residue, or a methionine residue.

29 (previously presented). The composition of claim 1, wherein the tetranectin trimerisation module has at least 68% sequence identity with the Trip A module (SEQ ID NO 13) and is capable of forming a stable trimeric complex with other tetranectin trimerising modules.

30-31 (cancelled).

32 (previously presented). The composition of claim 22, wherein the stable trimeric complex has a half-life at least 2 times the half-life of native apolipoprotein A-I, A-II or A-IV.

33 (previously presented). The composition of claim 22, wherein said stable trimeric complex is capable of binding to a receptor or protein selected from the group consisting of cubilin, megalin, Scavenger receptor class B, type 1 (SR-B1), ATP-binding cassette 1 (ABC1), Lecithin:cholesterol

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

acyltransferase (LCAT), Cholesteryl-ester transfer protein (CETP), and Phospholipid transfer protein (PLTP).

34 (cancelled).

35 (previously presented). The composition according to claim 33, wherein the trimeric complex comprises an amino acid sequence having at least 70% sequence identity to one of the sequences SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, SEQ ID NO 9, SEQ ID NO 10 or SEQ ID NO 11.

36 (cancelled).

37 (previously presented). The composition of claim 1, further comprising pharmaceutical acceptable excipients, adjuvants, or additives.

38 (previously presented). An apolipoprotein protein construct having the general formula

- apo-A-X,
- where apo-A is an apolipoprotein component selected from the group consisting of apolipoprotein A-I, apolipoprotein A-II, and apolipoprotein A-IV,
- and X is a tetranectin trimerising module.

39 (previously presented). The construct of claim 38, further comprising a spacer peptide between the apo-A component and the tetranectin trimerising module, wherein the spacer peptide comprises at least two amino acids.

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

40 (previously presented). The construct according to claim 39, wherein the spacer peptide is essentially non-immunogenic, and/or is not prone to proteolytic cleavage and/or does not comprise any cysteine residues.

41 (previously presented). The construct according to claim 39, wherein the three-dimensional structure of the spacer peptide is linear.

42 (previously presented). The construct according to claim 39, wherein the spacer peptide comprises an amino acid sequence selected from the group consisting of GTKVHMK (SEQ ID NO:69), PGTSGQQPSVGQQ (SEQ ID NO:70), GTSGQ (residues 2-6 of SEQ ID NO:70), PKPSTPPGSS (SEQ ID NO:71), SGGTSGSTSGTCST (SEQ ID NO:72), AGSSTGSSTGPGSTT (SEQ ID NO:73) and GGSGGAP (SEQ ID NO:74).

43-51 (cancelled).

52 (previously presented). The construct of claim 38, wherein the tetranectin trimerising module is part of a stable trimeric complex with two other tetranectin trimerising modules.

53 (previously presented). The construct of claim 52, wherein the stable complex comprises a coiled coil structure.

54 (original). The construct of claim 53, wherein the coiled coil structure is a triple alpha helical coiled coil.

55 (previously presented). The construct of claim 52, wherein the stable trimeric complex comprises two tetranectin

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

trimerising modules linked by a spacer moiety, which allows both of the two tetranectin trimerising modules to take part in the complex formation with a third tetranectin trimerising module not being part of the apolipoprotein protein construct.

56 (previously presented). The construct of claim 52, wherein the tetranectin trimerising module is selected from the group consisting of human tetranectin, murine tetranectin or C-type lectin of human, bovine or shark cartilage.

57 (previously presented). The construct of claim 52, wherein the tetranectin trimerising module comprises a sequence having at least 68% sequence identity with the sequence of SEQ ID NO 12 and is capable of forming a stable trimeric complex with other tetranectin trimerising modules.

58 (previously presented). The construct of claim 57, wherein the cysteine residue 50 in SEQ ID NO 12 is substituted by a serine residue, a threonine residue, or a methionine residue.

59 (previously presented). The construct of claim 52, wherein the tetranectin trimerising module has at least 68% sequence identity with the Trip A module (SEQ ID NO 13) and is capable of forming a stable trimeric complex with other tetranectin trimerising modules.

60-61 (cancelled).

62 (previously presented). The construct according to claim 103, wherein the trimeric complex comprises an amino acid sequence having at least 70% sequence identity to at least one

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

of the sequences SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, SEQ ID NO 9, SEQ ID NO 10 or SEQ ID NO 11.

63-84 (cancelled).

85 (previously presented). The composition of claim 22, wherein the stable trimeric complex has a half-life at least 3 times the half-life of native apolipoprotein A-I, A-II or A-IV.

86 (previously presented). The composition of claim 22, wherein the stable trimeric complex has a half-life at least 4 times the half-life of native apolipoprotein A-I, A-II or A-IV.

87 (previously presented). The composition of claim 22, wherein the stable trimeric complex has a half-life at least 10 times the half-life of native apolipoprotein A-I, A-II or A-IV.

88 (previously presented). The composition of claim 1, wherein the apolipoprotein A-I is human apolipoprotein A-I.

89 (currently amended). The composition of claim 1, wherein the apolipoprotein A-I is a fragment of human apolipoprotein A-I, where said fragment substantially retains the lipid binding function of human apolipoprotein A-I.

90 (previously presented). The composition of claim 89, wherein the fragment of human apolipoprotein A-I comprises at least the amino acids 100-186 of human apolipoprotein A-I.

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

91 (previously presented). The composition of claim 89, wherein the fragment of human apolipoprotein A-I comprises at least the amino acids 25-267 of human apolipoprotein A-I (SEQ ID NO 1).

92 (previously presented). The composition of claim 89, wherein the fragment of human apolipoprotein A-I is amino acids 68-267 from human apolipoprotein A-I.

93 (previously presented). The construct according to claim 38, wherein the tetranectin trimerising module is linked by a covalent link to the N-terminal or the C-terminal amino acid of apo-A.

94 (previously presented). The construct of claim 52, wherein the stable trimeric complex has a half-life at least 2 times the half-life of native apolipoprotein A-I, A-II or A-IV.

95 (previously presented). The construct of claim 52, wherein the stable trimeric complex has a half-life at least 3 times the half-life of native apolipoprotein A-I, A-II or A-IV.

96 (previously presented). The construct of claim 52, wherein the stable trimeric complex has a half-life at least 4 times the half-life of native apolipoprotein A-I, A-II or A-IV.

97 (previously presented). The construct of claim 52, wherein the stable trimeric complex has a half-life at least 10 times the half-life of native apolipoprotein A-I, A-II or A-IV.

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

98 (previously presented). The construct of claim 38, wherein the apolipoprotein A-I is human apolipoprotein A-I.

99 (currently amended). The construct of claim 38, wherein the apolipoprotein A-I is a fragment of human apolipoprotein A-I, where said fragment substantially retains the lipid binding function of human apolipoprotein A-I.

100 (previously presented). The construct of claim 99, wherein the fragment of human apolipoprotein A-I comprises at least the amino acids 100-186 of human apolipoprotein A-I.

101 (previously presented). The construct of claim 99, wherein the fragment of human apolipoprotein A-I comprises at least the amino acids 25-267 of human apolipoprotein A-I (SEQ ID NO 1).

102 (previously presented). The construct of claim 99, wherein the fragment of human apolipoprotein A-I is amino acids 68-267 from human apolipoprotein A-I.

103 (previously presented). The construct of claim 52, wherein said stable trimeric complex is capable of binding to a receptor or protein selected from the group consisting of cubilin, megalin, Scavenger receptor class B, type 1 (SR-B1), ATP-binding cassette 1 (ABC1), Lecithin:cholesterol acyltransferase (LCAT), Cholesteryl-ester transfer protein (CETP), and Phospholipid transfer protein (PLTP).

104 (currently amended). A trimeric complex ~~comprising an~~ consisting essentially of three apolipoprotein protein

Appln. No. 09/987,107

Amd. dated August 11, 2004

Supplementing Reply to Office Action of February 11, 2004

~~construct~~constructs, each construct having the general formula apo-A-X, where apo-A is an apolipoprotein component selected from the group consisting of apolipoprotein A-I, apolipoprotein A-II, and apolipoprotein A-IV, and X is a tetranectin trimerising module.